

EXTENDED REPORT

Behçet's disease in patients of west African and Afro-Caribbean origin

W Poon, D H Verity, G L Larkin, E M Graham, M R Stanford

Br J Ophthalmol 2003;**87**:876–878

See end of article for authors' affiliations

Correspondence to: Mr M R Stanford, Medical Eye Unit, St Thomas's Hospital, Lambeth Palace Road, London SE1 7 EH, UK; stanford@kcl.ac.uk

Accepted for publication 9 November 2002

Aim: To report the presence of Behçet's disease with ocular involvement in patients of west African or Afro-Caribbean origin.

Methods: Case series of eight patients reporting to a tertiary uveitis service.

Results: Eight patients with typical features of the disease are presented. Six of the eight patients were tested and found to be HLA-B51 negative.

Conclusion: Behçet's disease has only been reported in sporadic case reports in the indigenous west African and Afro-Caribbean populations, in whom the incidence of HLA B51 is also very low. A series of patients from the London region presented with the typical symptoms and signs of disease, most of whom were also HLA B51 negative. The presence of disease in this population, when absent in the indigenous population, suggests either that ascertainment of disease is poor in the indigenous population or that acquired factors may be important in the aetiology of the disease.

Behçet's disease (BD) is a chronic, relapsing, multisystem inflammatory disorder of unknown aetiology. The prevalence of disease is highest between latitudes 30° and 45°N in Asian and Eurasian populations¹ but is rarely encountered among individuals of central and west African descent. The genetic association of HLA B51 with BD is well described and may define disease risk, particularly for ocular involvement. It is not known whether environmental factors that might be experienced through a change in latitude may also influence disease risk in otherwise low risk individuals. We report a series of eight patients of west African or Afro-Caribbean origin presenting to two tertiary referral centres in London. Seven patients satisfied the International Study Group criteria for Behçet's disease.² In the other patient, with ocular and neurological involvement, typical histological changes were noted at necropsy.³ This series suggests that, while Behçet's disease is rare in patients of west African descent in Africa and the Caribbean,^{3–11} it may nevertheless occur in ethnic groups who were previously thought to have negligible risk of disease, and raises the possibility that environmental factors do contribute to the disease.

PATIENTS

Case 1

A 68 year old Afro-Caribbean male born in Jamaica presented with a painful right eye and decreased vision. For 2 years before his ocular symptoms, he had recurrent, painful oral ulcers, intermittent arthralgia of his wrists, ankles and dorsum of feet, and intermittent swelling of his left calf. He suffered from a scrotal ulcer in 1980 and also had an episode of left sided epididymitis. On examination, he had multiple ulcers in his right lower lip and tongue. Ocular examination revealed a panuveitis and an inferior branch retinal vein occlusion in the right eye. A diagnosis of BD was made and the patient was managed with oral prednisolone and azathioprine with resolution of the aphthosis and uveitis. Seven years later he developed a right popliteal aneurysm and underwent a femoral popliteal bypass procedure.

He developed cataracts in both eyes requiring surgery 16 and 18 years after his initial presentation. Four years later his visual acuity had dropped to counting fingers (CF) right eye and 6/12 left eye. The eyes were quiet but extensive macular

scarring and a pale disc were noted in his right eye, and old scars in the left. He continues to require oral prednisolone 5 mg once daily.

Case 2

A male Afro-Caribbean born in Jamaica in 1962 has been previously reported.² He presented with blurred vision in both eyes at the age of 26. Visual acuity at that time was 6/18 right eye and 6/9 left eye. He was found to have bilateral panuveitis and vitreous haemorrhage in his right eye. There were new vessels on both his optic discs. Investigations including Heaf test, Kveim test, chest x ray, and serum angiotensin converting enzyme (ACE) levels were normal. There was no history of breathlessness, skin lesions, arthralgia, or oro-genital ulceration.

His subsequent progress was marked by multiple neurological events. At the age of 27, he experienced a 2 week history of intermittent headache, vomiting, diplopia, drowsiness, low grade fever, and urinary incontinence. An enhanced computed tomograph (CT) scan identified a diffusely enhancing lesion in the left mid-brain. Cerebrospinal fluid examination was compatible with a tuberculoma (lymphocytosis, raised protein) and the patient was therefore commenced on antituberculous chemotherapy and 80 mg oral prednisolone with improvement of his symptoms. A year later he experienced further drowsiness and a repeat magnetic resonance imaging (MRI) scan showed the lesion had increased in size. Anti-TB treatment was stopped in view of the progression of the lesion and oral prednisolone was increased. Later that year he was readmitted with further deterioration of his neurological state and he developed a Gram negative septicaemia and died. Histological examination of the brain showed the characteristic features of Behçet's disease.

Case 3

A 41 year old Afro-Caribbean man born in Jamaica presented at age 31 with headaches. A diagnosis of sagittal sinus thrombosis was made. A year later he presented with oro-genital ulcers, arthralgia, fever and folliculitis, and 7 years later he suffered a deep venous thrombosis. He had become aware that his right vision was impaired 18 months before presentation. Treatment regimens had included azathioprine, tacrolimus, cyclosporin, and mycophenolate mofetil, but all were poorly

tolerated, and his compliance with oral prednisolone was poor. On examination, he saw CF right eye and 6/9 left eye. He had a mild bilateral anterior uveitis, and funduscopy revealed right optic disc pallor with marked vessel attenuation and fibrosis. Two weeks later the patient presented with a relapse in the left eye with a visual acuity of 6/24, a marked panuveitis, and retinal infiltrates. Oral prednisolone (1 mg/kg) was commenced and tapered but 1 month later he relapsed with a right hypopyon uveitis and no fundal view was possible. Oral steroid was increased to 50 mg again. At his most recent review his visual acuity had deteriorated to 3/60 right and 6/18 left. Both anterior chambers remained active, and a left vitritis was present.

Case 4

A 22 year old Nigerian female presented at the age of 20 with recurrent oro-genital aphthosis, arthralgia and episcleritis, and 2 years later developed a left anterior uveitis with a hypopyon. A month later she developed a panuveitis with retinal infiltrates in the same eye. Tests for the presence of HIV and tuberculosis were negative and she was commenced on oral steroid (prednisolone 1 mg/kg). A year later an acute uveitis with hypopyon developed in the right eye. Despite second line immunosuppression (azathioprine, cyclosporin A) her vision deteriorated further to CF. On review this year, her vision was perception of light (PL) right and hand movements (HM) left. Both anterior chambers remained active, the intraocular pressures were raised at 35 mm Hg, and there was marked bilateral vitritis. Mycophenolate mofetil was added to her regimen of cyclosporin, or oral prednisolone and topical timoptol and azathioprine were discontinued. At the most recent review, her visual acuity remained HM in each eye. However, there was marked reduction in the degree of intraocular inflammation and the intraocular pressure was controlled.

Case 5

A 43 year old man from Sierra Leone presented at age 35 with fever and rigors.⁸ He had erythema nodosum on his wrists, and oro-genital aphthosis. A diagnosis of Behçet's disease was made and the patient commenced on oral steroid. Five days later he developed an acute abdomen and multiple perforations of the caecum were found at emergency laparotomy. Histology of these lesions (neutrophilic vasculitis) was consistent with Behçet's disease; 5 years later, the patient was admitted with a 1 week history of malaise, fever, and headache, and a left hemiparesis. Oro-genital aphthosis was again present, and a mild bilateral anterior uveitis was also noted. A magnetic resonance imaging (MRI) scan identified a lesion extending from the right brainstem up through the right hemisphere. Neuro-Behçet's disease was diagnosed and the patient was commenced on oral prednisolone, azathioprine, and topical steroid treatment. Over the subsequent 2 years he suffered recurrent episodes of vitritis in his right eye

but maintained a visual acuity of 6/6. He remains in remission on prednisolone and azathioprine.

Case 6

A 31 year old Nigerian male born in the United Kingdom, presented with a gradual deterioration of vision in his left eye associated with recurrent painless episodes of redness and 2 months of blurring of his right vision. One year previously he had been diagnosed with a seronegative arthritis involving his ankles and oral aphthosis was noted at the time. Initial treatment was with oral sulphasalazine followed by oral steroid. On examination, his vision was 6/6 right eye and CF on the left eye. Ishihara colour testing was reduced in the left eye, and a left afferent pupillary defect was noted. There were 2+ vitreous cells in both eyes with marked vitreous haze in the left eye. Retinal examination showed extensive vascular sheathing, intraretinal infiltrates, bilateral cystoid macular oedema, and secondary left optic atrophy. On general examination oral ulcers, erythema nodosum, and arthralgia were noted, confirming the diagnosis of BD. At last follow up he was well controlled on prednisolone and azathioprine.

Case 7

A 41 year old woman born in Nigeria presented at age 34 with a 10 year history of oro-genital aphthosis and erythema nodosum. In addition, she had widespread folliculosis and arthralgia and was also noted to have bilateral anterior uveitis but with good vision. She has been controlled with azathioprine and colchicine without significant morbidity and her eye disease has not recurred.

Case 8

A 35 year old Caribbean woman born in Jamaica presented at the age of 32 with oro-genital ulceration. Three years later she developed folliculosis and bilateral vitritis but no retinal signs. Thus far only local symptomatic treatment has been required in order to control her disease.

DISCUSSION

The differential diagnosis of intraocular inflammation associated with systemic inflammation in patients of Afro-Caribbean descent should include sarcoidosis, tuberculosis, syphilis, Reiter's disease and HIV infection. This series reports eight patients of west African or Afro-Caribbean descent with Behçet's disease (Table 1). All patients were seen in a London hospital (accounting for 10% of the clinic population) and had resided in the United Kingdom for a number of years. The HLA status of six of the patients was known and all were B51 negative; this compares to a positivity rate of approximately 50% in our other patients. Their clinical progress was similar to European patients with the disease—namely, the refractory nature of ocular inflammation despite the use of modern immunosuppressive agents and a poor visual prognosis. In addition, the failure to recognise the typical features of the

Table 1 Clinical features of patients

Case No	Age at diagnosis	ISG criteria	Additional features	Length of disease to diagnosis	Treatment required	HLA-B51 status
1	45	Y	Aneurysm	2	Prednisolone/azathioprine	Neg
2	26	N	Neurological	3	Anti-TB/prednisolone	ND
3	31	Y	Thrombosis	0	Prednisolone/azathioprine/tacrolimus/mycophenolate/cyclosporin	Neg
4	20	Y	—	2	Prednisolone/cyclosporin/mycophenolate	Neg
5	35	Y	Intestinal and neurological disease	0	Prednisolone/azathioprine	Neg
6	30	Y	—	1	Prednisolone/azathioprine	Neg
7	34	Y	Arthralgia	10	Azathioprine/prednisolone/colchicine	Neg
8	32	Y	—	3	Topical prednisolone	ND

Table 2 World HLA-B51 prevalences among healthy control subjects: comparison between Africa (low prevalence of HLA-B51 in controls and low prevalence of Behçet's disease) and Middle East, Asia, and Far East (high prevalence of HLA-B51 and high prevalence of Behçet's disease)

Region	Country	Population or area	HLA-B51 (%)
Africa	Algeria		4.7
	Burkina Faso	Rimaibe	6
	Equatorial	Bubi	1.9
	Libya	Jewish	8.7
	Nigeria	West	2.6
	Gambia	Mandinka	2.4
	Sudan	Noba	2.2
	Sudan	Shiegia	23
	Zaire		4.1
	Zimbabwe		0.5
Middle East	Georgia	Georgians	13.7
	Georgia	Kurdish	16.2
	Iraq	Jewish	2.3
	Lebanon		6.1
	Palestine		15.3
Asia (cont)	China	North	2.5
	China	Han (South)	6.2
	Thailand	Central	7.7
	Tibet		13.4
	Vietnam		1.8
	China	Man (North East)	7.3
	China	Uygur (West)	8.8
	India	Punjabi	0
	India	North	7.6
	India	Iyers (South)	9.5
	India	North Delhi	13
	Japan	Mid	18
	Japan	South	22.3
	Korea		13
	Saudi Arabia		26
	Turkey		24

syndrome in this series of patients led to delay in diagnosis in three patients, and the diagnosis only becoming apparent at post mortem in another.

The aetiology of Behçet's disease is not known. It was first described in present day Turkey and is now widely recognised in countries bordering the Mediterranean, in Asia, and the Far East. This latitude gradient closely reflects the global distribution of the MHC allele HLA-B51 among healthy control populations (Table 2), and this allele is now recognised to be the greatest risk factor both for the development of disease and for the severity of ocular disease in a number of different populations. The exact role of the allele in promoting disease remains unknown. It is of great interest however that the prevalence of Behçet's disease is low both in central and west African populations, being limited to no more than eight reports of individual cases or short series,³⁻¹¹ and only one previous report has described patients from the Caribbean, all of whom were HLA-B51 negative.¹² Furthermore, at least two of the reports in the world literature describe patients resident in the United Kingdom,^{7,8} supporting the view that the true prevalence of disease in native African or Afro-Caribbean populations is very low indeed.

These observations may reflect the association between the prevalence of HLA-B51 among healthy control populations and the prevalence of disease in the same population. Review

of the distribution of the HLA-B51 allele among global populations (Table 2) reveals that this allele is infrequently encountered in central and west Africa, and therefore may account for the rarity of the disease in these populations. Data for the Caribbean black population are not available but may be assumed to be the same as data found in central Africa. Nevertheless, this report and others from the United Kingdom, indicate that the disease does indeed occur among people with genetic origins in these countries. The rarity of disease in Africa and the Caribbean may reflect a bias in case ascertainment, which depends on recognition of disease and access to medical care, but also suggests that a triggering agent for recurrent oral aphthosis, frequently the initial symptom of the disease, may be encountered in Europe to a greater degree than in central and western Africa. An analogous situation is seen in multiple sclerosis where individuals who are at low risk of disease in their country of birth assume a higher risk upon moving to more northern latitudes at a young age.¹³ Patients with BD described in this series were not all resident in the United Kingdom from childhood; nevertheless, a latitude dependent effect may explain why the majority of Afro-Caribbean patients have been described in northern climes.

In summary, it is becoming increasingly apparent that Behçet's disease is no longer limited to populations whose genetic origins lie on the old Silk Road. With increased demographic movement around the globe, it may be encountered in ethnic groups in which the disease was previously thought not to occur, and due consideration should be given to this in the differential diagnosis of severe intraocular inflammation, particularly in the presence of mucosal aphthosis.

ACKNOWLEDGEMENT

This work was supported by the Iris Fund for Prevention of Blindness.

Authors' affiliations

W Poon, D H Verity, E M Graham, M R Stanford, Department of Ophthalmology, St Thomas's Hospital, London, UK

G L Larkin, Department of Ophthalmology, Kings College Hospitals, London, UK

REFERENCES

- 1 Verity DH, Marr JE, Ohno S, et al. Behçet's disease, the Silk Road and HLA-B51: historical and geographical perspectives. *Tissue Antigens*. 1999;**54**:213-20.
- 2 International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's disease. *Lancet* 1990;**335**:1078-80.
- 3 Lueck C, Pires M, Graham EM. Ocular and neurological Behçet's disease without orogenital ulceration. *J Neurol Neurosurg Psychiatry* 1993;**56**:505-8.
- 4 Makene WJ. Behçet's syndrome with central nervous system involvement in a Tanzanian African. *East Afr Med J* 1969;**46**:199-203.
- 5 Raynor A, Askari AD. Behçet's disease and treatment with colchicine. *J Am Acad Dermatol* 1980;**2**:396-401.
- 6 Thomas I, Helmond ME, Nychay S. Behçet's disease presenting as superior vena cava syndrome. *J Am Acad Dermatol* 1992;**26**:863-5.
- 7 Jacyk WK. Behçet's disease in South African blacks: report of five cases. *J Am Acad Dermatol* 1994;**30**:69-73.
- 8 Taylor CB, Low N, Raj S, et al. Behçet's syndrome progressing to gastrointestinal perforation in a West African male. *Br J Rheum* 1997;**36**:498-501.
- 9 Lewis DA, Amerasinghe CN, Murphy SM. Successful treatment of Behçet's syndrome in an African female patient with thalidomide. *Int J STD AIDS* 1996;**7**:518-20.
- 10 Stein CM, Davis P. Arthritis associated with HIV infection in Zimbabwe. *J Rheumatol* 1996;**23**:506-11.
- 11 Wagaiyu EG, Chindia ML. Behçet's syndrome presenting with chronic periodontitis: a case report. *East Afr Med J* 1992;**69**:596-8.
- 12 Lannuzel A, Lamaury I, Charpentier D, et al. Neurological manifestations of Behçet's disease in a Caribbean population: clinical and imaging findings. *J Neurol* 2002;**249**:410-18.
- 13 Kurtzke JF, Delasnerie-Laupretre N, Wallin MT. Multiple sclerosis in North African migrants to France. *Acta Neurol Scand* 1998;**98**:302-9.